DOCUMENT RESUME

ED 247 731 EC 170 087

TITLE	Mental Retardation and Developmental Disabilities: 1981 Research Programs of the National Institute of Child Health and Human Development.
INSTITUTION	National Inst. of Child Health and Human Development (NIH), Bethesda, Md.
REPORT NO	NIH-82-2348
PUB DATE	Mar 82
NOTE	55p.; Prepared by the Mental Retardation and Developmental Disabilities Branch for presentation to the National Advisory Child Health and Human Development Council (May, 1981).
PUB TYPE	Information Analyses (070) -- Reports - Descriptive (141)
EDRS PRICE	MF01/PC03 Plus Postage.
DESCRIPTORS	Biological Influences; *Biomedicine; Developmental Disabilities; Environmental Influences; Family Relationship; *Federal Programs; Genetics; Interaction; Language Acquisition; *Medical Research; Memory; *Mental Retardation; Perceptual Development; Rehabilitation; Research Needs; *Social Science Research

ABSTRACT

The monograph reviews federal research activities and progress in biomedical and behavioral/social science research in mental retardation. Activities represent the National Institute of Child Health and Human Development and the Mental Retardation and Developmental Disabilities branch. The following categories are addressed in terms of biomedical research: genetics and genetic disorders (cytogenetics, inborn errors of metabolism); infection; toxicology and environmental factors (fetal alcohol syndrome, low level lead exposure); and congenital hypothyroidism. Areas of behavioral and social science research addressed are individual processes (cognition and learning, memory, perception, language, personality); family processes (parent-child interaction, parental attitudes, adaptive behavior); and residential and educational settings (social interaction, educational settings, research in institutions, group homes). Concluding sections consider research training and future research emphases in genetics/Down Syndrome, developmental neurobiology, high-risk infancy, and amelioration/rehabilitation. (CL)

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ED247731

1981

Research Programs
of the
National Institute of
Child Health and
Human Development

Mental Retardation and Developmental Disabilities

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

EC170187

Prepared by the Mental Retardation and Developmental Disabilities Branch for presentation to the National Advisory Child Health and Human Development Council, May 1981

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OVERVIEW

MENTAL RETARDATION

Few problems related to human development are more complex and challenging than mental retardation, a lifetime condition requiring study of the full range of developmental variables. Mental retardation weighs heavily on the individual, his family, the community and the economy and resources of the nation. The complex phenomena included under the term mental retardation, or MR, are the product of multiple interacting biological, behavioral, and social variables.

The task of bringing these phenomena together into a coherent body of related elements is similarly complex. Only by doing so, however, can we move toward an understanding of retardation and toward its prevention or amelioration. Involved are more than 6 million Americans who at some time in their lives will be labeled as mentally retarded.

For lack of a universal definition, estimates vary as to the prevalence of mental retardation. Based on the distribution of intelligence test scores, the traditional gauge, the number of mentally retarded in 1979 was put at 6.6 million Americans, or 3 percent of the general population. Some authorities, using more exclusive clinical criteria, estimate the number to be between 2.2 and 4.4 million persons, or 1 to 2 percent of the population. Higher estimates are made by those who include in their figures the less severely affected -- persons with IQ's up to 80 and with problems in social adaptation.

Mentally retarded individuals are classified into four groups according to their performance on standardized tests of intelligence. The mildly retarded are those with IQ's ranging from 52 to 70, the moderately retarded, from 36 to 51, and the severely retarded, from 20 to 35. Those with IQ's below 20 are considered profoundly retarded. Most mildly retarded children, who make up about 75 percent of the retarded population, are retarded from unknown causes. Many come from homes marked by deep stress due to poverty as well as family conditions sufficiently severe to lead to mild mental retardation. This type of retardation is called cultural-familial or psychosocial retardation. In recent years evidence has been accumulating that indicates that infants delivered prior to term, or who have a low birth weight or experience damaging events of pregnancy, birth or early infancy, are at greater risk for MR and other developmental disabilities. These infants, often referred to as "high-risk infants" or "infants at risk," are the subjects of many investigations concerned with the early development of children.

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

The National Institute of Child Health and Human Development is the primary locus at the National Institutes of Health for research concerned with maternal and child health. Within this broad mandate, the NICHD has primary responsibility for research and research training directed toward the problem of mental retardation and related aspects of human development. Since MR is a lifelong problem requiring study of the full range of developmental variables, it clearly illustrates the multidisciplinary mission of the NICHD. Mental retardation research at the NICHD is supported mainly through the Institute's Mental Retardation and Developmental Disabilities Branch (MRDD), in the Center for Research for Mothers and Children (CRMC). Other branches within the extramural and intramural programs of the NICHD have made significant contributions in the area with investigations into the damaging effects of aberrant pregnancies, difficulties during birth, and adverse factors in early infancy, as well as the effects of nutritional

deficiences and imbalances. Other more indirect contributions have been made through research aimed at improving the health of mothers.

To strengthen its research effort and to minimize duplication, the MRDD branch maintains close liaison with the other Federal agencies supporting research on MR. Prominent among these in the Public Health Service are the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the National Institute of Allergy and Infectious Diseases (NIAID) of the NIH; the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA); and the Bureau of Community Health Services (BCHS), Health Services Administration (HSA). The contributions made by the NINCDS primarily are in the area of developmental neurobiology and those of the NIAID, in the area of infectious diseases. In ADAMHA, the National Institute of Mental Health (NIMH) has research responsibility for the emotional and psychological aspects of MR. The BCHS supports health-related MR research of an applied type. In the Department of Education, the National Institute for Handicapped Research (NIHR) and the Office of Special Education and Rehabilitation Services also are sources of research support. The latter emphasizes research on educational methods. The former is a new agency in the process of establishing its priorities.

MENTAL RETARDATION AND DEVELOPMENTAL DISABILITIES BRANCH

The MRDD branch supports research and research training related to the biological, behavioral and social processes that contribute to or influence the development of retarding disorders. To accomplish its mission, the branch uses research grant mechanisms, supports special research facilities called Mental Retardation Research Centers (MRRC's), provides contract support for development of new research resources and disseminates information to the scientific community and the public.

Research on the causes, prevention and amelioration of MR contributes to the understanding of other developmental disabilities as well, including

autism, epilepsy and cerebral palsy, all of which are frequently associated with mental retardation.

More than half of the MR research supported by the MRDD branch is conducted in the MRRC's. The primary objective of the Mental Retardation Research Centers program is to provide facilities for a cohesive, interdisciplinary program of research and research training in MR and related aspects of human development. Currently there are 12 centers distributed throughout the nation. Their construction was authorized by Public Law 88-164, Title I, Part A. The NICHD has provided the centers with core grants (a program project grant mechanism) to facilitate program coordination and to support central facilities. In FY 1980, the centers received about $6.8 million in core grants. Total support for MRRC operations -- provided by the NICHD and other NIH institutes, other Federal agencies, foundations and other sources -- was approximately $30 million. About 15 percent of the total support to the MRRC's came from local sources.

Ten of the 12 centers are administratively and functionally joined with a University Affiliated Facility (UAF), supported, in turn, through the Bureau of Community Health Services and the Bureau of Developmental Disabilities. The UAF's were authorized by Public Law 88-164, Title I, Part B, to provide clinical training for the professions involved in treating mentally retarded individuals. They also provide a means for translating into services the new methods of treatment and care developed through research.

In its programming, the MRDD branch emphasizes research aimed at preventing MR, with special attention to elucidating the cause of Down syndrome, the most common genetically determined condition associated with mental retardation. Also given high priority are studies of "high-risk" infants, babies born under conditions associated with susceptibility to later developmental retardation. Family variables and parent (caregiver) interactions strongly influence the development of high-risk infants. Other influences included preschool and school and the larger community.

These factors often determine whether, as the child matures, he or she either drops from risk status or requires continued support to minimize residual deficits. Research that seeks to understand these processes and to find means to increase their positive effects on development is emphasized.

Research support is by no means limited to the above areas of special emphasis. More than 200 mental retardation syndromes have been identified, and new ones are discovered each year. Each requires fundamental research into the underlying processes, as well as studies designed to meet the unique needs of the afflicted children. Therefore, the branch supports a comprehensive program of MR research concerning the etiology and pathophysiology, epidemiology, diagnosis and evaluation, prevention and amelioration of mental retardation (table 1).

The following report describes research activities and progress in two major areas: biomedical research in MR and behavioral and social science research in MR. Tables 2 and 3 summarize the activities in these areas in terms of numbers of projects and funds allocated to their support. Approximately 62 percent of branch funds support biomedical research and 38 percent, behavioral and social science research. These figures are based on assignments of projects to areas of primary emphasis and do not reflect the interdisciplinary nature of many of the projects. A significant part of the branch's program involves both biomedical and behavioral scientists. Thus, some projects are listed in more than one category (table 2).

BIOMEDICAL RESEARCH IN MENTAL RETARDATION

GENETICS AND GENETIC DISORDERS

Improvements in nutrition, sanitation, the treatment of infectious disease, and the availability of vaccines and chemotherapeutic agents have

contributed to a shift in the pattern of disease in both young and old. Genetic disorders and congenital anomalies have emerged as issues of major health concern because of their relatively high frequency. These conditions are often encountered in surviving newborn infants and are commonly associated with MR.

The scope of the problem becomes apparent in the following data. Of live-born infants, an estimated 0.6 percent have major chromosomal defects such as Down syndrome; 1.8 to 2.0 percent, single gene defects such as phenylketonuria; and 1.7 to 2.6 percent, conditions believed to be of polygenic origin, exemplified by neural tube defects such as spina bifida.

The significance of these data for mental retardation may be seen in a 1970 study of 200,000 residents of institutions for the mentally retarded in the U.S.: In 20 to 25 percent of the cases, MR was attributable to genetic or genetically influenced conditions. Similarly, in a group of 122 Swedish children aged 5 to 16 with IQ's below 50, born in Uppsala County between 1959 and 1970, 43 percent were cases of genetic origin. Thirty-nine subjects (32 percent) had Down syndrome.

Cytogenetics

Chromosomes

The rapid advances occurring in cytogenetics research have added immeasurably to the understanding of genetic disorders. The advances are highly technical and require an understanding of chromosomes to be appreciated.

Chromosomes contain the genetic material of the cell and are located in the nucleus. In each normal human cell, except in ova and sperm, there are 46 chromosomes -- 44 autosomes and two sex chromosomes (two X chromosomes in the female, and one X and one Y chromosome in the male). The

chromosomes are photographed and arranged into 23 matching pairs, a process called karyotyping, to facilitate their study.

Chromosomes vary in size and shape. Karyotyping is based on these two characteristics. The largest pair of chromosomes is called number 1, the smallest pair number 22. The two sex chromosomes form the last pair in the karyotype. Each chromosome is composed of two identical nearly parallel strands joined at one short region called the centromere. Depending on the centromere's location, the upper and lower arms of a chromosome may be nearly equal in size or the upper segment may be shorter.

Down Syndrome

Down syndrome is the most common and readily identifiable genetic condition found among the mentally retarded. It falls into three genetic types depending on the chromosomal constitution: trisomy 21, translocation, and mosaicism. Trisomy 21 occurs in 95 percent of Down syndrome cases and is characterized by the presence of three, rather than the normal two, chromosomes in group 21. Trisomy results from nondisjunction, a genetic mechanism characterized by the failure of a pair of chromosomes to separate at meiosis (cell division), with the result that both members of the pair are carried to the same daughter cell and the other cell lacks that chromosome. Meiosis is the cell division that occurs in germ cells, or sex cells, in which the number of chromosomes found in somatic cells is reduced to one-half.

Translocation occurs in about 4 percent of Down syndrome cases. The number of chromosomes in the cells of these individuals is 46, but an extra chromosome in group 21 is attached (translocated) to another chromosome.

Mosaicism occurs in about 1 percent of children with Down syndrome. The abnormality derives from an error in the early cell division of a

fertilized ovum. An individual with this type of Down syndrome has cells with 47 chromosomes (i.e., trisomy 21) mixed with a varying proportion of normal cells.

Among 57,000 newborns in six surveys conducted between 1969 and 1975, the frequency of Down syndrome was one in 800 live births. Recent evidence suggests that the incidence of Down syndrome is declining. The reduction is attributed largely to two factors: progressively fewer babies born to women 35 years of age or older (the incidence of Down syndrome rises with maternal age), and the selective termination of pregnancy following prenatal diagnosis. In 1960, 10.9 percent of births in the U.S. were to women 35 years of age or older. In 1978, only 4.5 percent of births were to women in this age group. In a related statistic, the estimated number of babies born with Down syndrome in New York declined 20 percent between 1971 and 1975, after the state removed restrictions on terminating pregnancy in the first two trimesters of pregnancy in 1970.

Since proportionately more infants with trisomy 21 are born to women over 35, it is the mother that has been seen as the likely source of the extra chromosome. The assumption was based on the fact that all the ova a female ever has are present from birth and vulnerable, therefore, to the harmful effects of endogenous and exogenous agents, such as x-rays and infections. With the advent of new staining techniques, it is now possible to determine the parental source of the extra chromosome 21 in about 80 percent of Down syndrome cases. Using this technique, NICHD-supported investigators report that the father is the source of the extra chromosome in 23 percent of the cases studied. This finding has led to new approaches in genetic counseling and research design. Whereas research had focused almost exclusively on maternal factors, investigators now are turning their attention to paternal conditions that might contribute to the birth of a baby with Down syndrome.

The new staining techniques, which produce distinct alternating light-and-dark banding patterns on a chromosome, have enabled investigators

to pinpoint the segment of chromosome 21 responsible for the clinical and biochemical manifestations of Down syndrome. These characteristics are attributable to trisomy for a band located on the distal portion of the long arm of chromosome 21.

Beyond genetic counseling, parents of children with Down syndrome, particularly those of newborns, need information on new developments in the care, education, and management of the Down syndrome infant and child. Research and service advances have created conditions conducive to home care, public education, and a fuller role in community life for persons with Down syndrome. There has been a marked shift away from early institutionalization. Research supported by the MRDD branch has contributed to these developments, and continues to add knowledge in the area.

Significant contributions have come from the behavioral and social sciences. Behavioral research concentrates on speech and language, both characterized by relatively marked delay in the Down syndrome child. Studies are underway exploring how parent-child interactions influence language and cognitive development. Studies show that parents can teach their Down syndrome children. Research aimed at developing teaching tools for parental use is supported, as are studies of family variables which can contribute to the creation of an optimal home life for the child with Down syndrome. These activities are described in the section on the behavioral and social sciences.

Fragile X Syndrome

It is estimated that about 5 percent of moderately retarded males (IQ range 30 to 55) have the Fragile X syndrome, a type of X-linked MR. X-linked mental retardation is a hereditary abnormality with clinical manifestations limited almost exclusively to males. Females carrying the abnormal gene on one of the X chromosomes transmit the abnormal trait to 50 percent of their sons. The female carriers have a high incidence of mild mental retardation, but do not have the other clinical characteristics

observed in males with the syndrome. This syndrome appears to be the most common cause of MR in males; only Down syndrome causes more mental retardation associated with a chromosomal abnormality.

The Fragile X syndrome gets its name from the apparent instability of a portion of the X chromosome. A number of investigators, including scientists in NICHD-supported Mental Retardation Research Centers, are exploring the clinical characteristics of the syndrome. In males, these include mental retardation, verbal and auditory deficiencies, impaired fine motor control, hyperactivity, enlarged head in the absence of hydrocephalus, protruding chin, large malformed ears which are frequently lowset, and enlarged testes.

To develop diagnostic tests for Fragile X syndrome, NICHD-supported investigators are looking for the optimal tissue culture conditions needed to detect the abnormal X chromosome. They have demonstrated the chromosome in cultured skin samples obtained from carrier females and affected males. The findings provide a basis for reliable diagnosis of carriers and for prenatal diagnosis and genetic counseling. The Fragile X syndrome may help explain why approximately 50 percent more mentally retarded males than females appear among institutionalized and community-based subjects. Social and behavioral variables traditionally have been cited to explain this disparity.

Gene Mapping

Genes, the basic units of heredity, are located linearly on the chromosomes. In gene mapping one determines a gene's exact position on a chromosome. Gene mapping studies use somatic cell hybridization techniques, recombinant DNA techniques, and gene-linkage methods to characterize normal and abnormal chromosomes. Specific identifying traits corresponding to chromosomal deletions are also studied with immunological techniques. Human gene mapping is directed toward associating certain disorders with the absence in abnormality of a specific chromosome.

NICHD-supported investigators have identified and cloned fragments from the human X chromosome. This achievement will lead to better understanding of how the genes are organized and regulated on the human X chromosome, and will eventually enable scientists to identify the defective genes responsible for more than 150 X-linked human hereditary diseases. Already it is possible to detect markers linked to the defective genes. These markers can then be used to identify female carriers before the genes are passed on to their offspring.

Another group of investigators is mapping the genes on human chromosomes, looking at the specific distances between genes, how genes are recombined during meiosis, and how their expression is altered by their exact positions.

Research Resources

Animal model for genetic disorders -- Ethical restraints on research using human subjects, particularly studies involving minors, mentally retarded individuals or persons who cannot provide informed consent, have stimulated the search for suitable animal models. NICHD-supported investigators have demonstrated that two of the three genes located on chromosome 21 in man are located on mouse chromosome 16, suggesting a genetic homology between the two chromosomes. The investigators are breeding mice that produce litters trisomic for chromosome 16 as well as other chromosome groups. They also are developing techniques for freezing mouse embryos, some of which will carry specific chromosomal defects. The embryos can be reimplanted in pseudopregnant mice, and studies on their prenatal and postnatal development carried out. Storage, maintenance, and distribution costs are less for frozen embryos than for newborn or adult mice. Plans are under way to develop a mechanism for supplying the mouse model, including frozen embryos, to qualified investigators.

Automated chromosome slide preparation and karyotyping device -- Major deterrents to full application of cytogenetic knowledge have been

the time and effort required to perform chromosome analysis in the laboratory. To alleviate these problems, the NICHD has supported a project designed to develop an automated chromosome slide preparation and karyotyping device. The system, now undergoing field testing, will reduce the cost of cytogenetic diagnosis, expand genetic services to consumers, and permit broad-scale study of cytogenetic disorders, particularly those associated with environmental catastrophes. The devices can be used in research laboratories, clinical settings, and epidemiologic surveys.

Cytogenetic registry -- The MRDD branch supports a registry of cytogenetic, clinical and demographic information collected through the collaborative efforts of five laboratories across the country. The registry is used to develop uniform procedures for recording and storing information which can be used in more than one laboratory. Six research projects have been completed using registry data that demonstrate the feasibility of retrieving, collating, and analyzing stored information. The projects dealt with the frequency, type, and significance of "spurious cells" in amniotic cell culture; chromosomal rearrangement; the frequency of MR in Turner syndrome; the phenotype of patients with structural rearrangement of the X chromosome; and the rates of cytogenetic abnormalities diagnosed prenatally.

Data have been collected on approximately 34,000 patients, including more than 9,000 who underwent amniocentesis. The data base includes information on 3,084 trisomic, 213 partially trisomic and 111 partially monosomic individuals and those with other types of cytogenetic aberrations. An important aspect of the registry is that data can be retrieved based on different combinations of criteria such as age of ascertainment, cytogenetic aberration, and clinical manifestations. An announcement describing the registry and the availability of its data was published in the March 1981 issue of the NIH Guide for Grants and Contracts.

Inborn Errors of Metabolism

Phenylketonuria (PKU)

Phenylketonuria is an inborn error of metabolism in which the person is unable to metabolize phenylalanine, an amino acid essential to normal growth and development. It is associated with severe MR, behavioral problems, epilepsy and other signs of neurological impairment. The incidence of PKU is one per 14,000 births. Persons with untreated PKU invariably require long-term institutional care.

NICHD is contributing to the support of a collaborative study of children treated for PKU in 15 medical centers across the country. The study has demonstrated that when infants with PKU are treated with a diet restricting the level of phenylalanine, beginning within 120 days of birth and continuing until age 6, the child's growth pattern is normal for height, weight, and head circumference. The occurrence of congenital or neurological abnormalities among treated PKU patients is comparable to that among controls, the study shows. PKU subjects do not show more EEG abnormalities at age 6 than does the general population. Similarly, measures of intellectual development have shown that treated PKU children achieve scores comparable to those of normal children. The intellectual achievement of children treated within the first 30 days of life is significantly better, however, than that of children whose treatment is delayed. Investigators are now seeking to establish whether it is safe to discontinue the diet at age 6. Preliminary findings indicate no statistically significant difference in IQ at age 8 between children continuing the diet and those discontinuing it.

Programs screening for PKU in newborns are widely recommended. In the U.S., 43 states have laws requiring PKU screening. A 1974 survey of 117 institutions for the mentally retarded in the U.S. and Canada showed no admissions of children with PKU in states and provinces where newborns

were screened for PKU and where affected infants were put on the PKU diet soon after birth.

Maternal PKU

In the past, most phenylketonuric women of childbearing age were mentally retarded and bore few if any children. In the past 18 years, however, routine newborn screening and early treatment of PKU have resulted in normal physical and intellectual development among phenylketonuric girls, many of whom have normal capacity for conception. A woman with PKU who follows a regular diet during pregnancy most likely will bear a child with MR, congenital heart defects, intrauterine growth retardation or microcephaly, even though the child does not have PKU. The incidence of new cases of PKU-related MR could return to its former level after one generation if phenylketonuric women reproduce at a normal rate without dietary regulation of phenylalanine during pregnancy, thus offsetting the benefits of the neonatal screening program.

In an effort to learn what the mechanism is for these fetal effects and if they can be avoided with dietary restriction, the MRDD branch supports a maternal PKU project using rhesus monkeys. High blood levels of phenylalanine are induced in the mothers with a diet high in phenylalanine and a chemical that blocks the action of the metabolizing enzyme. Maternal and fetal blood phenylalanine, tyrosine and other free amino acid levels are monitored throughout gestation. The newborns are examined for congenital malformations and their development is assessed. Initial findings indicate that phenylalanine is readily transported across the placenta and the phenylalanine level in fetal blood is about 1.5 to 2.0 times higher than that in maternal blood. Thus, a phenylalanine level considered safe for the mother could be detrimental to the fetus.

Urea Cycle Metabolism

A defect in urea cycle metabolism, an example of another inborn error of metabolism, leaves an individual with a reduced capacity to synthesize

urea, the principal waste product of nitrogen metabolism. This disorder leads to an accumulation of ammonia and other nitrogenous precursors of urea which causes vomiting, lethargy, seizures and coma to develop within the first few days of life. The traditional treatment of removing the accumulated ammonia and its precursors through exchange transfusion, peritoneal dialysis or administration of nitrogen-free analogues of essential amino acids, has been unsuccessful. Most patients have died in infancy and survivors are usually mentally retarded.

NICHD-supported scientists have now developed a promising treatment for conditions characterized by nitrogen accumulation. They are using benzoic acid or phenylacetic acid, administered orally or intravenously, to facilitate excretion of the nitrogen by a new pathway. Although the treatment is being tested primarily in patients with abnormalities in urea cycle metabolism, it also may prove beneficial to those with other conditions characterized by an accumulation of nitrogen waste products, such as liver cirrhosis, Reye's syndrome and uremia.

Genetic Counseling

Genetic counseling is a communication process which deals with the human problems associated with the occurrence, or the risk of occurrence, of a genetic disorder in a family. The MRDD branch is supporting a field study of two groups of genetic counselors to identify the scientific, clinical, and social problems genetic counselors are faced with and the means they use to resolve them. In the study, a participant-observer records the interactions between a counselor and prospective parents to determine the patterns counselors follow in dealing with recurrent problems. In a second phase of the study, counseling style and patient comprehension will be assesssed. The study will provide information on: (1) the genetic counselors' perception and performance of their role, with emphasis on the approaches used to manage pressing clinical problems, and (2) the relationship of the process and dynamics of counseling to its outcome, as measured

by patient recall and comprehension, and patient attitudes before and after counseling.

INFECTION

Much is known about a number of infectious agents that contribute to MR, but it is not known what percentage of MR cases is related to infectious disease. Improved control of infectious disease has reduced the incidence of mental retardation and other handicapping conditions, but some infections -- cytomegalovirus (CMV) infection, for example -- remain problems.

An NICHD-supported project is investigating the pathogenesis and mode of transmission of CMV infection. CMV is the most common cause of congenital infection of the human fetus; 0.2 percent to 8.0 percent of newborns reportedly excrete the virus. Congenital CMV infection can result from primary maternal infection. Affected fetuses can be mentally retarded, low birth weight or suffer hearing loss. Often, however, congenital infections are subclinical.

The investigators have noted that stillbirth and widespread viral infection in newborn guinea pigs, the animal model used for the study, occurred more frequently if dams were infected in late gestation rather than in the first trimester. Although neonates of dams infected during early gestation did not have infectious virus, tissue destruction was observed in the kidneys, lungs and/or brains of 40 percent of the newborns examined, even when there was no detectable virus in these tissues.

To prevent congenital CMV infection, the female guinea pigs were vaccinated with either live virus or with vaccines prepared from viral membrane antigens. (An antigen is a substance which stimulates the production of antibodies.) Both vaccines offered protection against transplacental transmission of CMV and reduced the severity of primary infection during pregnancy. The live attenuated virus vaccine gave the greater protection against maternal and fetal infection.

It is not yet known whether the attenuated guinea pig or human CMV vaccines can reactivate during pregnancy. The investigators will continue the study to determine if live attenuated vaccines reactivate during pregnancy, revert to virulence, or result in transplacental transmission of the vaccine virus to offspring. Prevention of CMV infection by a vaccine will ultimately serve to reduce the incidence of MR.

TOXICOLOGY AND ENVIRONMENTAL FACTORS

Fetal Alcohol Syndrome

Investigators from a Mental Retardation Research Center were the first in this country to describe the fetal alcohol syndrome -- a pattern of malformation found in nearly half of the offspring of severely and chronically alcoholic women who consume alcohol throughout pregnancy. The clinical spectrum includes small head size, MR in more than 80 percent of cases, severe prenatal and postnatal growth deficiency, multiple joint contractures, congenital heart defects and facial abnormalities which permit recognition of the disorder during infancy. Since the prevalence of severe, chronic alcoholism during pregnancy is estimated to be 0.42 to 1.25 per 1,000 pregnancies, the number of fetuses at risk is considerable. Data from Seattle suggest that this syndrome may be the third leading recognizable cause of MR in that city.

Whether or not alcohol has a direct toxic effect on the developing fetus is unknown. Some other metabolite or nutritional deficiency associated with alcoholism may cause the damage. Preliminary observations suggest, however, that the alcohol itself, which freely crosses the human placenta, is the offending agent. Animal experiments in which other variables, such as nutritional status, were controlled have demonstrated alcohol-induced deformities and retardation of general growth. It is not known why some infants are normal and others severely defective when both are exposed to comparable amounts of alcohol in utero. Nor is it clear if

susceptibility to the teratogenicity of alcohol is genetically determined or attributable to intervening or interacting variables. The amount, duration, and regularity of alcohol consumption in pregnancy required to provoke this syndrome are not known.

Low-Level Lead Exposure

One of the most serious health problems for American children comes from exposure to lead. It has been estimated that as many as 600,000 children under age 6 show evidence of "undue lead absorption," i.e., blood lead levels of 30 to 69 ug/dl. Children who have had lead poisoning and recover are frequently left with profound developmental impairments, including MR, seizures, cerebral palsy or behavior disorders. Research is now drawing attention to the developmental effects of subtoxic lead levels.

An ongoing interdisciplinary study is exploring behavior and body lead levels in children who have no history of lead intoxication. Teachers' ratings, parents' ratings and cognitive performance are being compared in children with high (over 200 parts per million) and low (less than 8.5 parts per million) lead burdens. The index of body lead burden is based on the concentration of lead found in the dentine of shed deciduous teeth. Dentine, rather than blood, lead levels are measured because blood lead levels can return to normal relatively soon after exposure even when exposure is excessive.

Using an observational method to assess attention span in children in the third through sixth grades, the investigators have found that the high-lead group of children engaged in a variety of "off-task" behaviors significantly more often than did the low-lead group. Furthermore, the children's scores in a striking number of the observational categories were dose-related to lead. On a questionnaire containing 11 items related to classroom behavior, teachers gave high-lead children a significantly greater number of negative ratings on nine items. In general, these

scores also were dose-related to lead. Ratings made by the investigators based on observation in the classroom corresponded with the teachers' scores of children's behavior. On the Behavior Problem Checklist the frequency with which teachers reported "conduct problems" for the children was dose-related to lead. The group scores on the other subscales of this instrument did not differ.

Detailed examinations in a neuropsychological laboratory showed that children with high dentine lead levels were strikingly inferior to children with lower dentine levels with respect to IQ, verbal IQ, attention and auditory processing. The investigators concluded that low-lead exposure at doses below those producing symptoms severe enough for clinical diagnosis can lead to neuropsychologic deficits that may interfere with classroom performance.

CONGENITAL HYPOTHYROIDISM

The MRDD branch supports several projects dealing with perinatal factors and their neurologic sequelae (table 2), such as the effects of prematurity on intellectual and motor development. These topics are explored in greater depth by the Pregnancy and Perinatology Section, however, and will not be discussed here. The branch supports other types of biomedical studies, for example on congenital hypothyroidism.

Newborn screening programs involving more than 3 million infants have found that approximately one in 4,500 newborns has primary hypothyroidism. Less than 5 percent of those found to have the disorder were identified as suspects before screening.

Congenital hypothyroidism results in intellectual impairment and neurologic dysfunction unless diagnosed and treated early in infancy. An NICHD-supported project is seeking to establish a connection between improved intellectual development and early treatment of children with

congenital hypothyroidism identified by newborn screening programs. The study addresses three issues: (1) the relationship between age at onset of treatment and subsequent intellectual development; (2) the bearing on this relationship of factors such as varying concentrations of thyroid hormones, presence of clinical signs and symptoms and breast feeding; and (3) the predictive value of psychometric evaluations during infancy and the preschool years for subsequent intellectual development in children with the disorder.

BEHAVIORAL AND SOCIAL SCIENCE RESEARCH IN MENTAL RETARDATION

Behavioral and social science research supported by the MRDD branch falls into three major categories -- studies on individual processes, studies on family processes and studies of retarded people in educational and residential settings.

Historically, most of the research sponsored by the MRDD branch of NICHD has emphasized the retarded individual, and more than 50 percent of all federally funded behavioral research on mental retardation is concentrated in the area of individual processes. These studies have centered upon traditional fields of study in psychology: learning, cognition, perception and language. The goal of this research has been to characterize the range of behavior in mentally retarded individuals. Other studies have focused on intervention strategies designed to prevent or ameliorate mental retardation.

In the domain of family process research, increasing interest has been shown in the areas of how a mentally retarded child affects the family and how the family affects the retarded child. Perhaps, because the methodologies used in this area are still being developed, less than 20 percent of the research supported by the MRDD branch is related to family processes.

Finally, behavioral research in the MRDD branch focuses on retarded individuals outside the family, especially the retarded child in school and community-living settings. Because of the trend toward integrating retarded and developmentally disabled persons into the mainstream of society, social scientists have become increasingly interested in studying how these individuals adapt to community settings. More than a quarter of the behavioral research supported by the MRDD branch focuses on the retarded individual in settings outside the family.

The branch's behavioral research program spans the period from infancy to adulthood. Behavioral research in child development traditionally has been heavily concentrated on the infancy period, and the MRDD branch supports a number of studies on retarded infants. There has been a recent increase in such studies, however, possibly reflecting improved methods of early identification of retarded infants which makes it easier to locate them as subjects. The increase may also reflect the expansion of early intervention programs for handicapped infants.

These trends are partly a result of the application of research findings from NICHD behavioral and biomedical research programs to service delivery efforts. Research findings disseminated by the MRRC's have been applied in treatment programs for retarded individuals in many age groups and in settings outside schools; early intervention programs have also benefited from this research.

INDIVIDUAL PROCESSES

Cognition and Learning

In the past there has been great controversy centered on the structure of intelligence and specifically on how information processing by retarded individuals relates to intelligence. Mentally retarded individuals have a reduced capacity to learn and to process information, and until the past decade, researchers studying cognitive and learning processes in the

retarded focused on simple learning processes such as discrimination learning and various forms of conditioning. More recently, attention has been directed toward understanding how retarded individuals process information to solve specific problems. Computer technology has aided research in the area.

Several different approaches have been used in laboratories supported by the NICHD. One major change in the field has been the adoption of a developmental approach to learning and cognitive processes, stimulated by the wider acceptance of Piaget's and Bruner's "process" approach to intelligence and cognitive development. One investigator in a MRRC has been studying the usefulness of tests derived from Piaget's writings for testing institutionalized severely and profoundly retarded persons. This is an important series of studies since, generally, there is little useful information gained from standard intelligence tests with these groups of children. Results indicate that Piaget-based tests, which provide information regarding the process of learning, can be used to identify areas of cognition on which to focus educational programs. This research program should continue to provide important findings relevant to testing and teaching retarded persons. Another conceptual advance which has influenced researchers to focus on individual differences within the retarded population is the idea that development in retarded children proceeds at a different rate but follows the same progression as in normal children.

In recent years, the ability to identify developmentally disabled infants and those at risk for mental retardation has improved using methods developed in research with normal infants. Several investigators are comparing cognitive functioning in developmentally disabled infants and in those at risk for mental retardation with normal infants. Studies of intersensory integration as a predictor of later cognitive development in infants at risk for mental retardation are also under way. Other research has used the infant habituation procedure to study cognitive processing in high risk and retarded infants. In this procedure a stimulus

is presented repeatedly to an infant who is then tested to see if it can discriminate between the initial stimulus and other stimuli.

Several studies have shown that many infants from low-income families and infants with Down syndrome do not recognize visual forms as early as other infants. The Down infants also spend longer time initially looking at the pictures. These results suggest that, early in infancy, it may be possible to use testing techniques such as habituation to identify infants who are likely to be retarded learners. This possibility is strengthened by findings in other laboratories that habituation may be predictive of later intelligence in children.

There is a continuing controversy as to whether cognitive functioning in retarded individuals is marked primarily by developmental lag or developmental difference. Several investigators, who favor the developmental explanation for mental retardation, have demonstrated that both motivational and personality factors are responsible for the low level of cognitive performance in the retarded. Other investigators, who subscribe to the "difference" explanation, contend that retarded individuals are fundamentally different from nonretarded individuals in the way they learn. These scientists have been studying the ability of institutionalized retarded subjects to learn by extracting meaning from written material. Persons of lower intelligence appear to have limitations in their ability to attend to important aspects of learning situations; furthermore, it is difficult to change this basic characteristic in retarded persons.

Another characteristic exhibited by retarded children is that they do not seem to generalize learning to a wide set of problems and tasks. In one approach to this problem, an individual's awareness to the learning process is explored. This approach, called metacognition, has attracted many investigators. For example, one research team suppor ed by the MRDD branch has studied learning strategies in retarded and nonretarded children. These researchers have devised ways to teach some of these strategies to

retarded children and thereby improve their ability to learn. The researchers in this group are developing a new theory of intelligence which will have implications for teaching retarded children to learn more complex strategies in problem solving and to apply these strategies to a wider array of problems.

Several decades ago, social learning theorists suggested that a number of learning concepts might be applied to social behavior. One of these, imitation, has received some attention from mental retardation researchers. Investigators in two of the MRRC's have been studying how imitative behavior can be used to facilitate acquisition of a variety of skills, particularly among severely retarded children and youth who have been found to be unteachable using other learning strategies. The results have been encouraging. Other researchers studying cognition and learning in retarded children have discovered ways in which these children will learn in laboratory settings. At present, many of the researchers studying cognition are examining how retarded youngsters can be taught to generalize from laboratory learning to other situations. The development of generalized imitation in retarded learners promises to be an area which will continue to provide insights into the basic intellectual capacities of the retarded, as well as provide a basis for ameliorative efforts.

Memory

Individuals generally are judged to be intelligent if they are capable of recalling "facts" or information which they have learned previously. Similarly, standard tests of intelligence include items which test a person's memory, although it must be recognized that these provide only summary measures of performance under testing conditions.

Research designed to understand basic intellectual functioning among retarded individuals has traditionally been centered on how information is stored and retrieved from memory. Basic research on memory in the retarded is aimed at understanding the process by which information is

remembered and recalled. Many of the investigations referred to in the previous section involve processes which depend to some extent on memory ability. Fifteen percent of the projects and 17 percent of the funds for research on individual processes are focused on memory. In recent years there has been a shift from using older children as subjects to using younger children and infants. Some researchers are beginning to explore metamemory, i.e. awareness of the memory process, both in retarded infants and those at risk for retardation.

Other studies in this area are concerned with understanding the development of semantic memory (memory for meaning) in normal and retarded persons. One series of studies, being conducted at an MRRC, is focused on the form in which information is stored and retrieved by retarded individuals. These researchers have pioneered the development of methods for studying semantic memory that assess the unconscious automatic retrieval of semantic knowledge in the retarded. These methods have allowed the investigators to document similarities in memory skills between retarded and nonretarded individuals. In addition, the relationships between memory and the ability to make logical inferences are being studied. Some of this research is centered on so-called "executive" functions through which the individual selects and controls strategies for remembering or for committing information to memory.

Basic research on memory in the retarded is beginning to yield important results. Researchers supported by the MRDD branch have discovered that retarded individuals have difficulty transferring information from short-term memory to long-term memory and linking new information to previously learned material. Advances in computer technology have enabled scientists to experimentally manipulate strategies for remembering. Findings from this research indicate that retarded children do not store information in memory the way nonretarded people do but that it is possible to improve memory by teaching the retarded person how to remember information. Continued research in this area may soon lead to programs of teaching the

retarded how to remember things which will aid them in school as well as in everyday situations such as work, shopping and leisure activities.

Perception

Since information must be processed through the senses before it can be used to solve problems, understanding deficits in perception and perceptual-motor behavior of mentally retarded individuals is an important field of investigation. Investigators in two MRRC's are studying infant perception, including perceptual processes in different sense modalities of retarded infants and infants at risk for retardation. One project focuses on attention and attentional deficits in infants with Down syndrome and those at risk for mental retardation. This investigator has studied visual attention to nonsocial stimuli and now is investigating attentional processes used by high-risk and Down syndrome infants to perceive faces.

With technological advances that have made it possible to study eye movements, it is now possible to evaluate attention directed to different aspects of stimulus material and how individuals process the stimulus information. Researchers at one of the MRRC's have developed methods to study visual information processing in severely retarded persons and children at risk for mental retardation. Other studies of visual perception are focused on selective attention in retarded and autistic children and adults. Methods to assess visual acuity of retarded subjects are also being developed.

Several studies on perceptual processes focus on auditory perception -- an important prerequisite for language development. A number of researchers have been developing methods to assess auditory processing (listening and comprehension) skills in retarded children. Various forms of conditioning and behavior modification programs have been used quite successfully in this endeavor, and several projects supported by funds in the MRDD program use these methods. Auditory perception research includes studies on short and long latency auditory evoked potentials in retarded persons. In these

studies, measurements are made of retarded individuals' brain wave responses to auditory stimuli presented at different time intervals.

Research on perception in retarded and at-risk populations has led to understanding some of the dysfunctional and delayed development of retarded individuals by identifying specific deficits in perceptual processing abilities. This research has contributed to developing methods for identifying sensory and perceptual deficits which interfere with learning in the retarded. Future research will continue to concentrate on improving screening techniques in order to permit early identification of retarded individuals. In addition, research on perceptual processes will facilitate more refined research on cognitive and learning abilities among the retarded.

Language

In our complex and verbal society, language abilities are among the most important elements of adaptive behavior. Retarded individuals often are deficient in both receptive and productive language. Within the area of individual processes, language research is the focus of about a third of the projects supported by the MRDD branch. Research in the areas of language and communication disorders is being conducted in 8 out of the 12 MRRC's.

Studies range from experimental investigation of speech perception in infants to research in which language-retarded adults are trained to communicate using nonverbal methods. Methods used vary from the use of behavior modification techniques for training nonverbal children to psycholinguistic analysis of speech produced by mentally retarded persons.

Several investigators using "miniature language" systems have been studying the critical elements in language learning by teaching the language system to both retarded and nonretarded subjects. These studies have made it possible to understand better how language is learned by both retarded and nonretarded persons.

Several investigators are studying how the language processing ability of preschool children is related to subsequent reading readiness. Other researchers have devised methods for teaching language and reading skills to retarded learners. These projects rely heavily on the use of behavior modification methodology.

Two other research groups are engaged in descriptive analyses of language in naturalistic settings. They are interested in identifying the conditions under which maximal verbal output will occur. One study is analyzing the speech and communication patterns of profoundly and severely retarded persons. Subsequently, these researchers plan to design methods to optimize these behaviors as a way of improving the communication skills of retarded individuals.

The prominence of language problems among the mentally retarded requires a continuation and expansion of this research. More research needs to be done, for example, on alternative language systems with nonverbal retarded individuals. There have been great advances in teaching nonhuman primates to communicate through the use of such alternative language systems, and some researchers are adapting these methods to retarded individuals. Future research is expected to apply results from current receptive language studies to the area of language teaching of retarded persons. Ongoing longitudinal studies of language expression are expected to yield new information on the development of language in retarded infants, leading to greater understanding of the relationship of language to intellectual development.

Personality

One criterion for designating a person to be mentally retarded is evidence of significant problems in adaptive behavior. Currently, only 3 percent of the projects and 3 percent of the funds of the MRDD branch are directed toward research on individual processes. It is anticipated that more attention will be given to this area in the future.

Several projects are investigating personality factors in mental retardation. The effects of role-taking ability on cognitive functions and the development of self-image in retarded individuals have been studied. It was found that both past experience and cognitive factors affect role-taking ability and self-concept among retarded persons.

As noted earlier, there is a widespread effort to integrate retarded individuals into the mainstream of society. One major project was focused on determining whether personality variables are important to the successful integration of retarded children with nonretarded youngsters. Results suggest that mainstreaming does not affect the retarded child's expectation of success in school. This research has also compared personality characteristics of institutionalized retarded persons with those of nonretarded institutionalized individuals.

Some investigations in this research area are focused on personality and motivational factors in test taking. One group of investigators has been engaged in a series of studies in which they systematically vary test-taking conditions in order to examine the effects of these manipulations on performance on achievement tests and IQ tests. The conditions being manipulated are designed to decrease anxiety over taking a test.

Other studies have focused on a variety of personality factors, including introversion-extroversion, and the relationship of these traits to intellectual functioning. Most of this research is on children who are at risk for mental retardation.

The fact that there are few studies being conducted in the personality area suggests that this is a fertile area for development. Surveys of the literature indicate that there has been little research activity in the areas of motivation and personality as they relate to mental retardation. The paucity of research in these areas may indicate that the methodologies necessary to explore them in the context of retardation have not yet been

developed. Future staff activity will attempt to stimulate interest in the area of personality.

FAMILY PROCESSES

Research on family processes is the second major category of behavioral studies supported by the MRDD branch. These studies cover a variety of age groups from infancy to older retarded persons. Several longitudinal studies have been recently initiated. Other studies represent the culmination of more than 15 years of contact with a group of high-risk youngsters who were initially involved in an early childhood intervention program in the 1960's. Results of these studies indicate that the group who received early home and preschool intervention was unlikely to be placed in special education classes during their school careers. Six times as many children in the control group were in classes for the retarded when compared with the experimental group. This is strong evidence that preschool and home intervention is an effective way to prevent or reduce mental retardation. Other studies in the family process area concern parental attitudes and adaptive behavior.

Research on the families of retarded individuals has been minimal in the past, and the set of projects presently supported may represent the beginning of increased research in this area. It is clear that this whole area of investigation merits more attention. The effects of a retarded child on family structure, family functioning and family integrity, as well as the effects of these factors on the retarded individual, have been the focus of increasing concern by medical, behavioral and other health professionals. There is a need for a strong scientific base for intervention efforts designed to ameliorate the effects of mental retardation on the family.

Parent-Child Interaction

Research on parent-child interaction in families with retarded children has been limited in the past. As a result, little is known about the

actual transactions which occur between parents and retarded children. For the most part, studies in this area focus almost exclusively on mothers of retarded children, although several recent studies have included the father as well. A number of studies have examined the effects of intervention efforts with mothers of retarded or high-risk children. These studies generally involve global or "ecological" interventions in which the children are placed in an environment designed to provide training for the child in several behavioral domains.

One of the basic descriptive studies in this area is a 1 year developmental investigation of two groups of infants at risk for mental retardation -- premature infants and full-term but small-for-gestational-age infants. Relationships between the mothers' behavior and the infants' arousal state and respiration, including respiration during sleep, are being examined. Two other studies recently have been started in which infants with Down syndrome and both of their parents are being followed during the first 2 years of the children's lives. One of these studies focuses exclusively on verbal interaction while the other one is concerned with a variety of parent and infant behaviors.

Another longitudinal study of infants and mothers is examining the relationship between individual differences in high-risk infants and their behavioral interaction with their mothers. Another investigator is concerned with exploring how infants at risk for mental retardation perform on the Brazelton Newborn Behavioral Assessment Scales in relation to their behavior in face-to-face interaction with their mothers. This longitudinal study is designed to document the course of development among infants at risk for mental retardation. The outcome of this research will provide useful information on whether the ways in which parents behave with their young children are influenced by the children's being at risk for mental retardation or developmental delays. These results will have important implications for the treatment and management of infants who are born with indications of significant impairment. The results of these studies will

permit further understanding of the role of specific environmental factors on the development of infants who are subsequently identified as being mentally retarded.

In addition to the many basic research projects focused on the role of parent-child interaction in the prevention and treatment of mental retardation, the MRDD branch has been supporting research on behavioral interventions designed to prevent mental retardation. Several of these projects have shown that early educational intervention is very effective in preventing mental retardation. One intervention project, now in its eighth year, has sought to prevent mental retardation among a sample of high-risk rural infants by providing a full-time educational day care program for the first years of the infants' lives. A behavioral intervention project of this kind is similar to a randomized clinical trial since it includes random assignment to treatment and control groups. The behavioral treatment group is exposed to an intervention program designed to prevent mild mental retardation.

The investigators on this project also observed mother-infant interactions over a period of time. Based on these observations, the researchers reported that the level of intellectual development within the high-risk sample was predicted by maternal behavior toward the infant as well as by maternal attitudes about development. Another report from this project indicates that mothers of high-risk infants interacted less with their children during ages 2 and 3, and that the quality of the interactions did not improve. These results suggest that although the intervention program affected the children's intellectual performance, it did not alter the mothers' behavior with their children.

A number of projects focus on interventions in which parents of retarded or high-risk children, rather than the children, are the target of the intervention. These projects are based on the assumption that parents can provide more effective behavioral intervention for the children than can professionals. One project is presently evaluating the results

of parental training more than a decade after the intervention took place. The children in this study were from low-income homes and were considered at risk for familial retardation. These children are now finishing high school and some are parents themselves. Early intervention efforts with the parents of these children seems to have affected whether or not these youngsters were placed in special education classes during their school years. This suggests that the intervention may have motivated the parents to encourage their children's school achievement and performance.

Other projects on parent-child interaction are concerned with training parents of developmentally disabled children. Some of these studies have demonstrated that children with Down syndrome progress more when trained by their parents than when trained by professional educators. Other researchers have been developing programs to teach parents of retarded children how to handle behavior problems.

Research findings thus far have shown that, with guidance, mothers of retarded infants and children may be the most effective trainers of their children. Under ordinary circumstances, the mothers often will be so involved in play with their children that the children themselves will scarcely have a chance to develop social and affective skills. Results indicate that when the mothers are instructed to match their behavior with that of their children. the children will be more likely to develop verbal skills, a basic requisite for learning. Another major achievement indicates that in some families, where opportunities for experience are limited, the children may benefit from structured school experiences from early infancy. Research has shown that such interventions do not disrupt the family as some have predicted.

Finally, a small number of projects supported by the MRDD branch use animal models to study parent-offspring interaction. These include primate studies in animals known to be either at high-risk or low-risk for reproductive problems. These primates are studied after giving birth in order

to determine if reproductive problems influence subsequent parenting behavior. Paternal as well as maternal factors are being studied in this research. Detailed examination of the effects of birth conditions on parent-infant relationships are also included in this project.

Other parent-offspring animal studies included a rabbit model of high-risk infants as well as projects utilizing a wide variety of rodent species. In the past, animal models have been quite successful in developing hypotheses about parent-child relationships which could be subsequently tested in humans. It is expected that these animal studies of parents and their offspring will continue to provide models of parent-child interaction.

Parental Attitudes

Although it is well known that a person's attitudes do not necessarily predict his or her behavior, studies of attitudes can often shed light on how an individual tends to behave. Often attitudinal measures may be obtained when direct assessments of behavior are not possible. Parental attitudes regarding an array of factors related to mental retardation have not been explored as extensively as might be expected.

The research currently supported in this area is focused on parental attitudes toward rearing high-risk or developmentally disabled children. Some of the findings from these studies indicate that mothers who have high self-esteem tend to have positive attitudes toward their high-risk children and positive perceptions of their children's sociability. These studies also find that maternal perception of the children's sociability is positively related to the children's verbal intelligence and academic performance, but not to the children's self-concepts in kindergarten and first grade. Another investigator has found that when parents are divided into "successful" and "average" groups, according to staff ratings of family integration, the mother's self-confidence and positive attitudes toward work and the couple's parenting differentiate the two groups. These results are being explored in depth. The purpose of this research

is to try to define dimensions which differentiate the ability of parents of retarded children to adapt successfully to their children's condition.

Adaptive Behavior

The ability to adjust one's behavior to changes in the environment is one of the criteria used to judge a person's competence. Recent classifications of mental retardation are based on assessment of limitations in both intellectual functioning and adaptive behavior. One researcher supported by the branch, suggests that there are three major components of a child's adaptive behavior: (1) competence; (2) socialization; and (3) temperament. He also suggests that these components have different antecedents and correlates. This investigator is actively developing a conceptual model of adaptive behavior in relation to family process. Present evidence indicates that mother-child, father-child, and mother-father relationships are correlated with the child's social adjustment. It is hoped that further analysis of adaptive behavior in children and of family environments may lead to a better understanding of the factors that influence the development of mentally retarded children.

Another project, part of a longitudinal study of children at risk for retardation, has found that differences in the adaptive behavior of high-risk children are related to their ability to cope with stress in the environment. Other work in this area has looked at whether family adaptation problems vary as a function of age, sex and birth order of the handicapped child and whether social support networks can lessen the stress caused by the child's handicap. One of these projects included a sample of autistic children who also showed signs of being mentally retarded. Results indicated that the older children were more difficult to manage than the younger ones when birth order, gender, and other important factors were controlled.

Conclusions from various studies on the adaptive behavior of developmentally disabled children suggest that a variety of characteristics,

such as repeated unusual behavior, lack of responsiveness, and demands for care, can predict family stress. Other studies support the conclusion that several parental stress factors are related to the child's ability to adapt successfully. Future work by these investigators will continue to focus on theoretical formulations of the adaptation of retarded children and their parents to each other. Results of these studies also may provide important information which can be used in clinical intervention programs and may provide the bases for ameliorating conditions which contribute to mental handicap.

In general, research which has focused on behavior of retarded children in families has shown that the family can be a major resource for ameliorating the effects of mental retardation and developmental disabilities. However, a family with limited adaptive resources can be so stressed that the child is prevented from developing optimally. In these instances, structured, educationally oriented interventions are successful in facilitating optimal development in the retarded child but only when there is an effort made to include the family in intervention.

RESIDENTIAL AND EDUCATIONAL SETTINGS

Behavioral research in mental retardation traditionally has been conducted in institutions for the retarded and in educational settings. About one-fourth of the behavioral research supported by the branch is conducted in settings outside the family. Research in this area is divided into four categories. The largest group of studies focuses on social interaction and includes research in a variety of settings. A few studies are assessing the adjustment made by retarded persons who are living in group homes in the community. About 25 percent of the projects in this area are focused on retarded individuals in an educational setting while an equivalent number are conducted in institutions for the retarded. These latter two groups of studies are concerned with the special characteristics of the settings which relate to the behavior of retarded individuals.

In general, most research in settings outside the family has been descriptive. Now, investigators are beginning to test specific hypotheses based on this descriptive work. Testing these hypotheses may provide information which will improve the quality of life and health for the retarded individuals in settings outside the family.

Social Interaction

Research on social interaction of mentally retarded persons employs many methods and covers a wide spectrum of characteristics of the groups studied. Methods range from interviews with caregivers and retarded individuals aimed at understanding social interaction patterns of the retarded, to observations of interactions between retarded individuals and between retarded and nonretarded persons. Recent laws which mandate mainstreaming of handicapped individuals into nonsegregated settings have prompted wide-ranging interest in the social integration of disabled persons. Some investigators have focused on the earliest social contacts between retarded and nonretarded toddlers. Results of these studies indicate that unless adults intervene or there are procedures designed to encourage interaction, the retarded childen tend to remain isolated. Other studies designed to measure the importance of imitation as a social influence have shown that nonretarded children do not imitate retarded children and that retarded children do not necessarily benefit socially from their contact with normal children. Based on some of this work, investigators at several of the MRRC's have shown that training either retarded or nonretarded preschoolers to initiate and respond to one another greatly enhances the social exchanges between the children. Other studies have been successful at decreasing antisocial behaviors while increasing social interaction among retarded youngsters in play settings.

At one of the Mental Retardation Research Centers, a group of investigators is studying social interaction in the neighborhoods of children who are at risk for familial mental retardation. Preliminary findings

indicate that, in contrast with low-risk children, the high-risk children engaged in less verbal interaction and less social play. No differences were found in aggressive or negative interactions between the two groups. These findings are somewhat at odds with reports that high-risk children are more disruptive in school. This study is unique, however, in its focus on children in neighborhood settings. It is expected that this kind of research will be pursued more vigorously as observational methods become more widely used and as more investigators are trained to study retarded individuals in natural environments.

Other investigators have used animal models of retardation to study social interaction. Some of these projects include studies of interactions among monkeys who have been raised in deprived environments. Results from this research indicate that the effects of deprived environments depend upon differences between species as well as upon the relevance of social interaction to the reproductive and parenting behaviors of the particular animal.

Basic research on social interaction among mentally retarded persons is fundamental to understanding how intellectual capacity affects other aspects of behavior. Investigators studying the relationship between cognitive and social behavior in nonretarded individuals have discovered that many of the theories which have been of interest in research on cognitive functioning also are useful in the study of social competence. More extensive investigations in this area are needed in order to further explore the extent to which limited cognitive skills also limit an individual's ability to adapt socially. Advances have been made in applying behavioral technology to the integration of retarded individuals into mainstream society. It is of major importance that, as the result of some of this research, retarded individuals are able to participate in the world outside residential settings. With the help of research findings, practitioners have developed programs for training social skills in retarded children and adults so that these individuals will "fit into" society.

Further research on social interaction will lead to better understanding of individual differences in social aspects of retarded development.

Educational Settings

Research on retarded persons in educational settings has been an area in which there has been extensive research. Much of the research on mentally retarded persons in schools is supported by the Department of Education. However, some research on basic and applied topics in this area has been supported by the NICHD in the past and continues to receive modest support. Much of the NICHD-supported research has focused on the infancy and early childhood period, which traditionally has received little support from other agencies. Studies on basic social interaction between retarded children and academic personnel have also been supported by the MRDD branch.

Several investigators are studying how ecological and behavioral factors affect learning and academic achievement of retarded children in school. A number of other studies have focused on special educational interventions which were designed to modify behavior among retarded children. In many of these research programs, researchers have designed intervention strategies and allowed teachers to implement the programs. Research on the relationships between teacher characteristics and child characteristics have also been conducted.

In several longitudinal research projects, the impact of several forms of instruction have been studied to evaluate the psychological variables on which interventions can be based. Attempts also have been made to evaluate specific aspects of the global or "ecological" intervention programs which have been successful in preventing retardation among the children in the programs. In one of these programs, the relative contribution of school and home based educational interventions is being studied.

Several researchers have been trying to determine the best way to apply findings from basic research on learning to school settings in order

to increase the academic performance of retarded children and adolescents. Some of these scientists are taking advantage of advances in computer technology to increase the learning potential of retarded individuals. Research in educational settings provides the opportunity to test applications of basic research findings obtained in the laboratory. These studies allow continued progress in educational technology. Results of applied research stimulate further laboratory research on learning and cognition. It is expected that continued developments in computer technology will present new opportunities to ameliorate mental retardation in school settings.

Research in Institutions

Retarded individuals have been kept in state operated institutions for many decades in order to provide them with what was thought to be cost-effective services. Until very recently it was believed that no other alternative living arrangement would be as satisfactory for fulfilling the state's obligation to care for handicapped individuals. However, during the past decade a variety of forces has led to efforts to decrease the populations in these large institutions. Unfortunately, research on optimal living environments has been limited and many policy decisions have been made in the absence of a strong empirical base. Researchers supported by NICHD funds have been studying the residents and the environmental conditions in these institutions. For example, they have been analyzing the treatment programs in these facilities and studying the influence of size and quality of the institutions on the quality of life for the residents. Much of this research is directed toward development of adequate methods to study individuals in institutions.

One grantee has been investigating visual and tactile exploration of toys by severely retarded residents of a state institution. It was found that it was possible to increase the amount of time and the level of contact made with toys by manipulating the conditions and time under which they

were available. This research was stimulated by similar studies conducted in infant day care centers in one of the MRRC's.

Surprising differences in mortality statistics have been found for retarded persons living in state institutions as compared with those living in community convalescent homes. Substantially higher mortality rates were found in the convalescent homes. Several researchers have been studying the reasons for this unexpected finding. This and other studies on institutional care have revealed that there are aspects of state institutions which might be more beneficial to residents than alternative living settings. Continued research into conditions and practices in institutional settings is necessary to gather data on which to base treatment decisions.

With the trend toward community placement of former residents of institutions for the retarded, the remaining residents consist mostly of severely and profoundly retarded persons. Some of these individuals are unable to walk or care for themselves although a large proportion can get around and have some self-help skills. The most remarkable research finding is the discovery that many of these individuals are capable of much more than was previously thought. They can learn; they can benefit from training experiences; and they are capable of making and keeping friends. For many years these individuals were ignored by scientists because it was felt that they were incapable of complying with most study demands. It is clear that future research on institutionalized retarded persons will focus on their capabilities. As a result there should be great improvements in the quality of life in these institutions and improved health for the residents. It is expected that a moderate level of research in this area will be funded in order to find solutions to questions regarding the care and health of severely retarded individuals who must be cared for in institutions.

Group Homes

Alternative living environments such as small group homes for the retarded have become the focus of behavioral studies because of the recent

trend away from housing retarded persons in large institutions. Although only a small number of projects on group home living currently are supported by the branch, there has been continual interest in this topic and an increasing number of research applications over the past few years. The focus of the research on homes ranges from studies of peer interaction to investigations of conflict and problem solving. Descriptive data on the ability of retarded persons living in group homes to manage daily life tasks are being collected in one study. That investigator has made an effort to select group homes which vary in size and structure in order to evaluate the effects of several different living arrangements on behavior. In another study, measurements of skill level, physical health, and behavior were made before the residents were randomly assigned to new living arrangements. Thus, the effect of changing living environment, the influence of size and composition of social groups, biological factors, and changes in opportunity to interact can be empirically evaluated. Research on group home residents must be expanded in order to understand better how limitations in mental functioning affect a person's ability to develop independent living and working skills.

The major findings of research on retarded persons living in group homes indicate that there is a great variability in the behavior of the residents. This variability depends on the severity of retardation with the most retarded individuals showing the most maladaptive behavior including low levels of social interaction, high levels of bizarre behavior, and limited learning ability. Group homes offer researchers an opportunity to study many variables related to adaptive behavior without the negative influence of institutional deprivation. Efforts are being made to encourage investigators to initiate research in these alternative residential settings and to develop research strategies which are appropriate for such settings.

RESEARCH TRAINING

The MRDD branch supports a substantial research training program to prepare investigators for research careers in the field of mental retarda-

tion and related aspects of human development. Institutional training grant awards providing both pre- and postdoctoral stipends are the mainstay of the branch's training award program. In FY 1980, the branch supported 14 institutional training grants which provided training for 89 predoctoral and 47 postdoctoral trainees. Predoctoral training support is greater for the behavioral and social sciences than the biomedical. In FY 1980, 8 of the 14 institutional training grants provided training for 70 of the 89 predoctoral trainees in the behavioral and social sciences. Six of the institutional training grants were in MRRC's, emphasizing interdisciplinary training in addition to training in specific areas of scientific specialization.

Individual postdoctoral research training grant awards are made and serve to complement the institutional training grant program. In FY 1980, the branch supported three research fellowships in areas of immediate relevance to important problems in mental retardation.

FUTURE RESEARCH EMPHASES

The plans of the Institute for meeting the complex problem of mental retardation have been developed as part of the Institute's Five-Year Research Plan. This plan calls for sustained program efforts with major emphases as follows:

GENETICS/DOWN SYNDROME

The Institute's concern with mental retardation resulting from genetic causes is expressed in its future plans. Research in genetics with emphasis on Down syndrome has been designated as an area for future expansion. The broad goal of this program is to achieve fundamental understanding of the basic mechanisms involved in the determination of genetic disorders. Within this framework, specific efforts will be directed toward achieving understanding of the fundamental processes of nondisjunction as a cause of

Down syndrome. It is anticipated that development of the mouse model for trisomy 21 and its deployment to investigators will serve as a resource for expanded research on this problem. Increased knowledge of the mechanisms involved in nondisjunction will result in a better understanding of Down syndrome as well as many other cytogenetic disorders associated with nondisjunction.

Expanded efforts are planned to resolve the research problems posed by the Fragile X syndrome. The broad goal of this program is to elucidate the causes and the clinical and behavioral characteristics of the syndrome. Specific efforts call for the initiation of epidemiological studies to define the phenotype, determine the optimum tissue culture which might maximize identification of the Fragile X chromosome, and to investigate methods appropriate for the development of prenatal diagnostic technology.

The Institute's program of research on inborn errors of metabolism will study galactosemia and urea cycle metabolism with emphasis given to the emerging new problems of maternal phenylketonuria.

DEVELOPMENTAL NEUROBIOLOGY

Research on the developmental neurobiological aspects of mental retardation has been maintained at a strong level of support. Future plans provide for this program to be sustained with particular emphasis being given to fundamental research into neurobiological, neuroanatomical, neurochemical and neuropharmacological processes related to mental retardation.

HIGH RISK INFANCY

The Institute has had a program of research concerned with the early identification of infants at risk for becoming mentally retarded and with development of intervention methods designed to reduce the degree of risk.

Continuation and expansion of this program is planned. The objective of this program is to establish firm criteria of risk status for biologically and environmentally vulnerable infants so that they can be provided with appropriate behavioral and biomedical intervention serving the purpose of primary, secondary, and tertiary prevention. A second objective is the further development and refinement of effective intervention methods.

AMELIORATION/REHABILITATION

Lessening the damaging effects of mental retardation and finding means for rehabilitation of persons afflicted with the problem is a major objective of the Institute. Research plans concerned with this issue embrace studies of the effects of deinstitutionalization both on the individual and on his/her family; study of effects of depriving environments upon psychobiological development; investigation of alternative patterns of care such as foster homes; development of rehabilitative and training technologies; and studies of parent-infant child transactions as these can contribute to improved development for the retarded person.

Presently, there are no major projects which are concerned with studying the behavior of retarded individuals in work settings. The workplace presents an opportunity to test a variety of hypotheses regarding the role of mental retardation on productivity and how retarded persons can contribute more to society while leading a more satisfying life. Although there has been some activity in this area in the past, interest has been minimal in recent years. Continued efforts will be made to stimulate research projects which provide basic data on relevant variables in work settings which might be used in improving retarded performance.

Table 1. MRDD grants and contracts by program category, FY 1980.

Funds (thousands)

Program Category	Total	Research Grants				National Research Service Awards	Research Contracts
		Total Research	Research Projects	Program Projects	Res. Career Awards		
Total	$27,407	$24,842	$6,323	$18,342	$177	$1,774	$790
Etiology/Pathophysiology	13,841	12,751	3,653	9,028	71	858	232
Epidemiology	706	563	536	27	--	143	--
Diagnosis and/or Evaluation	8,288	6,956	1,576	5,274	106	774	558
Prevention	1,155	1,155	192	963	--	--	--
Amelioration-Education	2,424	2,424	228	2,196	--	--	--
Amelioration-Medical Treatment	951	951	139	812	--	--	--
Other	43	43	--	43	--	--	--

Number of Projects

Program Category	Total	Research Grants				National Research Service Awards	Research Contracts
		Total Research	Research Projects	Program Projects	Res. Career Awards		
Total	522	492	76	416	5	21	4
Etiology/Pathophysiology	298	286	50	234	2	11	1
Epidemiology	7	5	3	2	-	2	-
Diagnosis and/or Evaluation	144	133	17	113	3	8	3
Prevention	17	17	2	15	-	-	-
Amelioration-Education	32	32	2	30	-	-	-
Amelioration-Medical Treatment	22	22	2	20	-	-	-
Other	2	2	-	2	-	-	-

NOTES: (1) Excludes four scientific evaluation grants for $153,000.
(2) Subprojects of program projects are counted individually.

Table 2. MRDD branch projects in the biomedical sciences, FY 1980.

Category	Number	Funds
Genetics and Genetic Disorders	156	$7,450,580
Cytogenetics	23	1,559,394
Inborn Errors of Metabolism	89	4,731,957
Research Resources	21	1,315,329
Genetic Counseling	9	221,481
Other Genetics	14	937,748
Infection	7	355,648
Toxicology and Environmental Factors	37	2,187,604
Perinatal Factors and Neurological Sequelae	59	2,051,266
All Other Biomedical	111	4,751,832

Table 3. MRDD branch projects in the behavioral and social sciences, FY 1980 (dollars in thousands)

Category	Number	Funds
Behavioral and Social Science Research	165	$9,330
Individual Processes	102	5,380
Cognition and Learning	77	4,353
Memory	15	903
Perception	30	1,601
Language	33	1,658
Personality	3	181
Down Syndrome	6	380
Family Processes	24	1,538
Parent-Child Interaction	20	1,350
Parent Attitudes	2	71
Adaptive Behavior	3	218
Down Syndrome	2	87
Residential and Educational Settings	39	2,413
Social Interaction	29	1,616
Educational Settings	10	884
Institutions	11	957
Group Homes	2	195

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Publication No. 82-2348
March 1982